

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT


(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CPW/20725	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA416)	
International application No. PCT/GB 03/04734	International filing date (day/month/year) 03.11.2003	Priority date (day/month/year) 04.11.2002
International Patent Classification (IPC) or both national classification and IPC C07D277/B2		
Applicant CIPLA LTD. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 12.05.2004	Date of completion of this report 22.10.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Allard, M Telephone No. +31 70 340-2002



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/GB 03/04734**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-6 as originally filed

Claims, Numbers

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-19
	No: Claims	-
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-19
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	-

2. Citations and explanations

see separate sheet

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EXAMINATION REPORT - SEPARATE SHEET**

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Reference is made to the following documents:

- D1: EP-A-0 186 087 (DR. KARL THOMAE GMBH) 2 July 1986 (1986-07-02)
D2: ALLINGER J ET AL: "The conformers of 2-bromocyclohexanone"
TETRAHEDRON, vol. 2, 1958, pages 64-74, XP002253277
D3: ALLINGER N L ET AL: "Conformational analysis. II. The 2-bromo-4-t-
butylcyclohexanones" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol.
80, no. 20, 20 October 1958 (1958-10-20), pages 5476-5480, XP002253278

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial
applicability; citations and explanations supporting such statement**

Novelty (Article 33(2) PCT)

None of the available prior art documents discloses the preparation of 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole by a series of reactions comprising bromination of 4-acetamido-cyclohexanone *in water*: the subject-matter of claims 1-19 is therefore novel.

Inventive step (Article 33(3) PCT)

D1, which is considered to represent the closest prior art, describes the preparation of 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole by bromination of 4-acetylaminocyclohexanone in acetic acid, reaction of the obtained compound with thiourea, and deacetylation with HBr, see examples 3 and 4.

In the light of the teachings of D1 the problem underlying the present application can be seen in the provision of a further process to prepare 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole.

To solve this problem the present application proposes to perform the bromination step in aqueous solution.

It is however already known from D2 and D3 that bromination of cyclohexanones can be performed in aqueous solution, see D2, paragraph bridging pages 71 and 72, and D3, page 5478, right-hand column, first paragraph.

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The proposed solution appears therefore to be an obvious measure in the design of an alternative process. As all further measures recited in the claims are known from D1 or obvious, the subject-matter of claims 1-19 lacks an inventive step.

It has been submitted that the above-mentioned bromination in aqueous solution *without isolation of the brominated compound* leads to an unexpected improvement in the overall process: as however this specific feature of not isolating the intermediate compound is not recited, explicitly or implicitly, in the claims, it cannot be taken into account for assessing the inventive step.

In this context it should be noted from the wording of claim 2, that the term "adding" used in claim 1 does not necessarily imply that the compound produced in the preceding step is not isolated. Moreover, even the use of a single reaction vessel, as recited in claims 3 or 4, does not preclude isolation of the different intermediates.

Industrial applicability (Article 33(4) PCT)

The processes of claims 1-19 can be used in the chemical, particularly pharmaceutical, industry.